

## REMARKS

Claims 1-30 are currently pending in the present application. Claims 1 and 25-30 are the only claims in independent form. The claims have been amended consistent with suggestions set forth in the Office Action and to correct minor typographical errors. In addition, the claims have been amended in order to remove non-elected subject matter as set forth in the Office Action. These amendments do not constitute new matter. Applicants reserve the right to file divisional applications pursuing the non-elected subject matter.

Specifically referring to the Office Action, claims 1-24 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for prodrugs of the compounds of formula (I). In response thereto and in order to expedite the allowance of the present application, the term "prodrugs" has been deleted from the claims. As a result, reconsideration of the rejection is respectfully requested.

Claims 1-24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Number 6,011,155 to Villhauer (hereinafter, "the '155 patent.") According to the Office Action, the only difference between the presently claimed invention and the compounds disclosed in the '155 patent is that R1 of the present claims represents alkyl, while the '155 patent represents hydrogen. Therefore, according to the Office Action, it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results.

In response to the outstanding rejection, Applicants argue that the cited prior art neither discloses, suggests, or motivates to modify the cited prior art to provide for the claimed invention. More specifically, the prior art discloses various modifications at the 1 or 2-carbon position of the pyrrolidine ring, but the cited prior art references do not disclose or suggest the introduction of a substituent at the 5-carbon position of the pyrrolidine ring. In contrast, the presently claimed invention is directed towards substitutions at this position. As a result of these substitutions, different qualitative activities are provided by the presently claimed invention. In fact, the various compounds disclosed in the presently claimed invention demonstrate unexpected activity against human DPP-IV enzyme and/or rat DPP-IV enzyme. As set forth in the specification, the compounds of the present invention were found to inhibit DPP-IV induced fluorescence with inhibitory constants in a range of about 0.014  $\mu$ M to about 7  $\mu$ M. In addition,

little was known about the effect of additional substitutions on the pyrrolidine ring. Thus, with the present invention, it was shown that substituents at the 5-carbon position of the pyrrolidine ring leads to compounds with superior selectivity profiles. Differences in potency were demonstrated between an unsubstituted 5-carbon and a substituted 5-carbon (e.g., methyl) on the pyrrolidine ring in the enclosed paper authored by the inventors (please see Table One of J.Med. Chem. 2006, 49, 6416-6420). Therefore, since the prior art neither discloses, suggests, nor motivates the modification of cited prior art and unexpected results exist with regard to the substitution of the 5-carbon position of the pyrrolidine ring, the obviousness rejection has been overcome. Reconsideration of the rejection is respectfully requested.

Claims 1-24 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of co-pending U.S. Patent Application Number 11/036,258 to Madar, et al. In response thereto and pursuant to 37 C.F.R. § 1.321, a terminal disclaimer is included herewith in order to overcome the rejection. Specifically, the terminal disclaimer identifies the patent application and term being disclaimed, states the present extent of the patentee's ownership interest, has been signed by an attorney of record, and is accompanied by the required fee. Additionally, a declaration is included herewith confirming that both pending applications are commonly owned. Reconsideration of the rejection is respectfully requested.

Claims 1-24 have been objected to as containing non-elected subject matter. In response thereto and in order to expedite the allowance of the present application, these claims have been amended to delete non-elected subject matter. Applicants reserve the right to file divisional applications to pursue the non-elected subject matter. Reconsideration of the objection is respectfully requested.

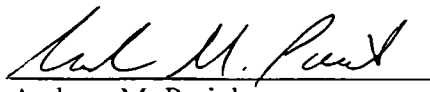
Claims 6, 10, 12, 16, 18, 20, 22, and 24 have also been rejected due to typographic errors of the last second compound of each of claim. According to the Office Action, the insertion of the term "and" would obviate the objection. In response thereto and pursuant to the suggestion set forth in the Office Action, the term "and" has been added to all of these claims. Reconsideration of the objection is respectfully requested.

In summary, the present amendment places the present application in condition for allowance, which allowance is respectfully requested. If any remaining issues exist. Applicants respectfully requests to be contacted through the undersigned below.

The Commissioner is hereby authorized to charge any additional Filing Fees required under 37 CFR §1.16, as well as any patent application processing fees under 37 CFR §1.17 associated with this communication for which full payment had not been tendered, to Deposit Account No. 01-0025.

Respectfully submitted.  
Madar. et al.

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